

It is claimed:

*Subj 5*  
1. A system for picking up a plurality of submillimeter beads from a bead supply and transferring them to a desired location, comprising:

a plurality of projections depending from a support at spaced-apart locations defining an array;

a cavity formed at a lower end region of each of said projections, each of said cavities defined by (i) a lower opening, (ii) an upper ceiling region, and (iii) a sidewall extending between said lower opening and upper ceiling region; and

10 an attraction source, operable at said projection end regions, effective to draw beads from said supply into said cavities and to releasably retain them therein.

2. The system of claim 1, wherein said sidewall is comprised, at least in part, of a resiliently flexible material.

15 3. The system of claim 1, wherein each cavity has a substantially constant diameter along a region extending between its lower opening and its upper ceiling region, such that lines extending longitudinally along confronting inner surfaces of each sidewall are substantially parallel to one another.

20 4. The system of claim 1, wherein the diameter of said lower opening is between about 100-1,250 micrometers and the longitudinal length of said sidewall, from said lower opening and to said upper ceiling, is between about 0.50-1.25 times the diameter of said lower opening.

25 5. The system of claim 1, wherein the diameter of said lower opening is between about 250-750 micrometers and the longitudinal length of said sidewall, from said lower opening and to said upper ceiling, is between about 0.75-1.10 times the diameter of said lower opening.

30 6. The system of claim 1, wherein said cavity is dimensioned to receive at least half of one submillimeter bead, and to preclude entry therein of a substantial portion of a second such bead.

7. The system of claim 1, further comprising  
a plurality of ampules for containing said bead supply, said ampules disposed  
in an array alignable with said projection array.

5 8. The system of claim 7, further comprising  
a plurality of covers, each cover configured to extend over an upper opening  
of one of said ampules.

9. The system of claim 8, wherein each of said covers is a frangible membrane.

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10. The system of claim 7, wherein said support is held by a frame that is  
(i) adapted to pivot about a generally vertical axis, rendering movable said  
projection array along a generally arcuate or circular pathway, and  
(ii) adapted for reciprocal linear motion along a generally vertical pathway;  
such movement permitting said projections to be aligned with said ampule  
array and lowered so that each projection can enter a respective one of said  
ampules.

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11. The system of claim 7, wherein one of said ampules holds a plurality of  
submillimeter beads that carry a first set of analyte-specific reagents, and another of  
said ampules holds a plurality of submillimeter beads that carry a second set of  
analyte-specific reagents; said first and second reagent sets differing from each  
other by at least one analyte-specific component.

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12. The system of claim 2, wherein said resiliently flexible sidewall has a  
generally cylindrical shape, with both an inner diameter and a longitudinal depth of  
between about 100-1,250 micrometers.

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13. The system of claim 12, wherein said inner diameter and longitudinal depth  
are between about 350-425 micrometers.

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14. The system of claim 1, wherein said cavity is formed by a resiliently flexible,  
tubular sleeve fit over the end of a respective projection, said sleeve having an  
overhang region extending below a terminal end of said projection defining said

sidewall; and wherein said terminal end of said projection, facing said cavity, defines said upper ceiling region of said cavity.

15. The system of claim 1, wherein each of said projections is a capillary tube  
5 having an axial lumen extending therethrough, each lumen having (i) a first end that opens into a respective one of said cavities through said ceiling region, and (ii) a second end disposed in fluid communication with a pressure-control assembly.

16. The system of claim 15, wherein said pressure-control assembly includes (i) a  
10 vacuum pump operable to establish a reduced pressure within each of said lumens, said reduced pressure defining said attraction source; and (ii) a pump operable to establish an increased pressure within each of said lumens, said increased pressure effective to displace any beads retained in said cavities.

15 17. The system of claim 15, wherein each of said lumens has an inner diameter at said first end that is smaller than the diameter of a respective cavity at a location directly adjacent said ceiling region.

20 18. The system of claim 17, wherein each of said cavities has an inner diameter at a location directly adjacent said ceiling region of greater than 275 micrometers, and each of said lumens has an inner diameter at said first end of between 100-275 micrometers.

19. The system of claim 1, further comprising  
25 a detection system having a field of view extending along each of said projection end regions, and adapted to sense the presence or absence of a bead retained in said cavities.

20. The system of claim 19, wherein said detection system includes a plurality of  
30 elongated light-conductive fibers, each fiber having one end that extends along one of said projections and faces said cavity, and a second end disposed in optical communication with a camera device.

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21. The system of claim 1, further comprising  
a conduit assembly having a plurality of conduits for separately channeling a  
plurality of submillimeter beads released from said cavities to desired locations on a  
substrate, said conduits having (i) large openings at their upper ends disposed in an  
array having a center-to-center pitch like that of the projection array such that the  
large openings are generally alignable thereunder, and (ii) small openings at their  
lower ends.

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22. The system of claim 21, wherein said small openings are disposed in an array  
having a center-to-center pitch substantially smaller than that of the large-opening  
array.

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23. The system of claim 22, wherein the center-to-center pitch of the small-  
opening array is reduced by a factor of at least about 3, as compared to that of the  
large-opening array.

24. The system of claim 21, wherein said substrate is a micro-card having a  
plurality of wells disposed in an array alignable under said small-opening array.

25. The system of claim 24, further comprising  
a detection system having a field of view extending into each of said conduits,  
and adapted to sense the presence or absence of a bead in each well of said micro-  
card.

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26. A system for channeling a plurality of submillimeter beads to desired locations  
on a substrate, comprising:  
an array of micro-bead supports, each support adapted to releasably hold,  
from above, no more than one submillimeter bead;  
a plurality of conduits disposed under said micro-bead support array, said  
conduits having (i) large openings at their upper ends disposed in an array having a  
center-to-center pitch like that of the support array such that the large openings are  
generally alignable thereunder, and (ii) small openings at their lower ends.

27. The system of claim 26, wherein each of said large openings has a diameter of less than about 6mm, and each of said small openings has a diameter of less than about 0.6mm.

5 28. The system of claim 26, wherein said small openings are disposed in an array having a center-to-center pitch smaller than that of the large-opening array.

10 29. The system of claim 28, wherein the center-to-center pitch of the small-opening array is reduced by a factor of at least about 3, as compared to that of the large-opening array.

15 30. The system of claim 28,  
wherein the center-to-center pitch of the large-opening array is greater than about 4mm, and the center-to-center pitch of the small-opening array is less than about 3mm.

20 31. The system of claim 26, further comprising a parallelogram linkage assembly supporting said conduit array for reciprocal arcuate movement between a raised position and a lowered position.

25 32. The system of claim 31, further comprising  
(i) a carousel adapted for rotation about a central axis, said carousel (a) pivotally supporting said parallelogram linkage assembly for movement radially of the axis of rotation of the carousel, and (b) having a substrate holding area adjacent to said parallelogram linkage assembly; and  
(ii) a stationary rail extending along an inner region of said carousel and having a continuous bearing surface in mechanical communication with said parallelogram linkage system, said bearing surface having (a) a region disposed a first distance from said central axis and at a first vertical height, whereat said conduit array assumes said lowered position over said substrate holding area, and (b) a region disposed a second distance from said central axis, shorter than said first distance, and at a second vertical height, higher than said first vertical height, whereat said conduit array assumes said raised position.

33. The system of claim 26, wherein said substrate is a micro-card having a plurality of wells disposed in an array alignable under said small-opening array.

34. The system of claim 33, wherein said micro-card is provided with a pair of spaced-apart indexing holes, each being alignable with a respective indexing pin depending from a lower side of said conduit array; whereupon registering said indexing pins in said indexing holes substantially aligns said small-opening array with said micro-card well array.

35. The system of claim 26, further comprising a detection system having a field of view extending into each of said conduits, and adapted to sense the presence or absence of a bead on said substrate under each of said small openings.

36. The system of claim 35, wherein said detection system includes a radiation source adapted to illuminate said substrate at locations below each of said small openings; and a plurality of elongated light-conductive fibers, each fiber having (i) one end disposed to receive light traveling up through a respective conduit, and (ii) a second end that communicates with a camera device.

37. An apparatus for delivering a substance onto a substrate, comprising: a plurality of elongated conduits disposed in fixed, spaced relation in a common support structure; each of said conduits having a large opening at one end and a small opening at its other end; wherein said large openings are disposed in an array along one side of said support structure, and said small openings are disposed in an array along an opposite side of said support structure; wherein said large-opening array is arranged with a center-to-center pitch larger than that of the small-opening array; and wherein a region of each conduit extending from a respective one of said small openings is of capillary size, such that a liquid placed in contact with said

small-opening array can be drawn at least partially into said conduits by way of capillary action.

38. The apparatus of claim 37, wherein said capillary-size region of each conduit 5 has an inner diameter of less than about 1mm.

39. The apparatus of claim 37, wherein said capillary-size region of each conduit has inner sidewalls that are hydrophilic.

10 40. A method for simultaneously transferring a plurality of submillimeter beads from one location to another location, comprising:

(i) picking up simultaneously a plurality of submillimeter beads from a supply and retaining the beads at respective, spaced-apart locations defining an array;  
(ii) releasing the beads, in a substantially simultaneous fashion, over a substrate having an array of separate bead-holding regions; and  
(iii) individually channeling each of the released beads, in a substantially simultaneous fashion, into a respective one of said bead-holding regions.

41. The method of claim 40,

20 wherein said array of bead-holding regions has a center-to-center pitch substantially smaller than that of the retained-bead array.

42. The method of claim 41,

25 wherein the center-to-center pitch of said array of bead-holding regions is reduced by a factor of at least 3, as compared to that of the retained-bead array.

43. The method of claim 40,

wherein said supply is provided in an array of ampules, each having a cover over an upper opening thereof;

30 and further comprising, prior to step (i), gaining access to said beads by displacing, at least in part, each of said covers.

44. The method of claim 40, further comprising:  
between steps (i) and (ii), inspecting each location of said retained-bead array for the presence of a bead; and, if a selected number of beads are missing, picking up and retaining a bead for locations lacking a bead.

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45. The method of claim 40, further comprising:  
after step (iii), inspecting each of said bead-holding regions for beads deposited therein.

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46. The method of claim 45, further comprising  
covering each of said bead-holding regions with an optically clear film.

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47. The method of claim 40, wherein  
said step of picking up beads is effected by establishing a reduced pressure at each of said locations, and said step of releasing said beads is effected by establishing an increased pressure at each of said locations.

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48. The system of claim 19, wherein said detection system includes at least one image capture device positioned to capture and display an image that includes the lower end region of each of said projections to provide an indication of the presence or absence of a bead retained in the lower end region cavity of each projection.

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49. The system of claim 48, wherein said detection system includes a pair of image capture devices.

50. The system of claim 48, wherein the captured and displayed image further provides an indication of whether more than one bead is retained in the lower end region cavity of any projection.

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